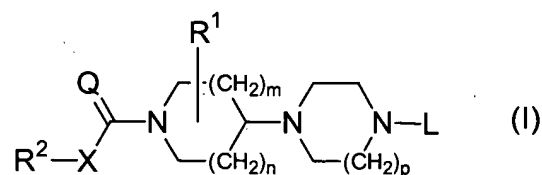


Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredients, an opioid analgesic and a therapeutically effective amount of a compound according to Formula (I)



the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the *N*-oxide form thereof and the prodrugs thereof, wherein

n is 0, 1 or 2;

m is 1 or 2, provided that if m is 2, then n is 1;

p is 1 or 2;

$$=Q \quad \text{is } =0 \text{ or } =NR^3;$$

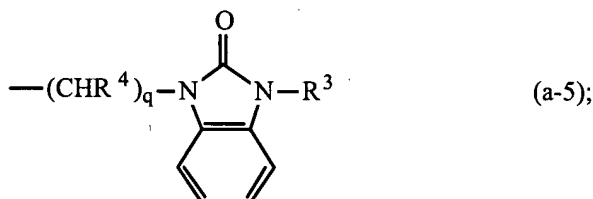
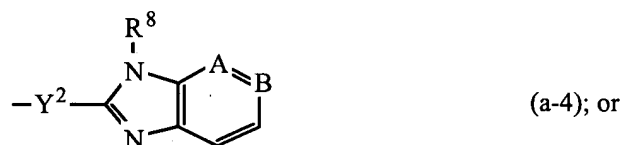
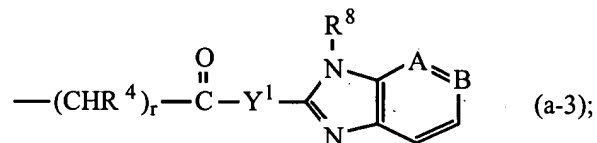
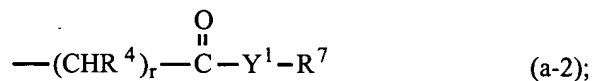
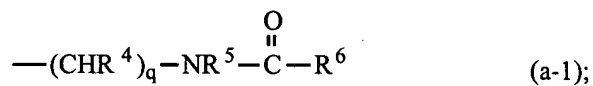
X is a covalent bond or a bivalent radical of formula -O-, -S-, -NR³-;

R¹ is Ar¹, Ar¹C₁₋₆alkyl or di(Ar¹)C₁₋₆alkyl, wherein each C₁₋₆alkyl group is optionally substituted with hydroxy, C₁₋₄alkyloxy, oxo or a ketalized oxo substituent of formula -O-CH₂-CH₂-O- or -O-CH₂-CH₂-CH₂-O-;

R² is Ar², Ar²C₁₋₆alkyl, Het¹ or Het¹C₁₋₆alkyl;

R³ is hydrogen or C₁₋₆alkyl;

L is hydrogen; Ar³; C₁-6alkyl; C₁-6alkyl substituted with 1 or 2 substituents selected from hydroxy, C₁-6alkyloxy, Ar³, Ar³C₁-6alkyloxy and Het²; C₃-6alkenyl; Ar³C₃-6alkenyl; di(Ar³)C₃-6alkenyl or a radical of formula



wherein

each q

independently is 2, 3 or 4;

each r

is 0, 1, 2, 3 or 4;

each Y¹

independently is a covalent bond, -O- or NR³;

Y²

is a covalent bond, C₁-4alkanediyl or -C₁-4alkylNR³-;

each -A=B-

independently is a bivalent radical of formula -CH=CH-, -N=CH- or -CH=N-;

each R⁴

independently is hydrogen, C₁-6alkyl, Ar² or Ar²C₁-6alkyl;

R⁵

is hydrogen, C₁-6alkyl or Ar³;

R⁶

is C₁-6alkyl, Ar³, Ar³C₁-6alkyl, di(Ar³)C₁-6alkyl, Ar³C₃-7cycloalkyl, or indolyl;

R⁷

is Ar³; Ar³C₁-6alkyl; di(Ar³)C₁-6alkyl; C₁-6alkyl; C₃-7cycloalkyl; C₃-7cycloalkyl substituted with Ar³; oxazolyl; oxazolyl substituted with halo or C₁-6alkyl; thiazolyl; thiazolyl substituted with halo or C₁-6alkyl; imidazolyl; imidazolyl substituted with Ar³, C₁-6alkyl,

each R⁸ is Ar³C₁₋₆alkyl or halo; indolyl; indolyl substituted with C₁₋₄alkyl; 2,3,4-trihydroquinolyl; pyrrolidinyl or furanyl; independently is hydrogen, C₁₋₆alkyl, C₃₋₇cycloalkyl or a radical of formula of formula

-Alk-R¹¹ (b-1) or
-Alk-Z-R¹² (b-2);

wherein

Alk is C₁₋₆alkanediyl;

Z is a bivalent radical of formula -O-, -S- or -NR³-;

R¹¹ is phenyl; phenyl substituted with 1 or 2 substituents selected from halo, C₁₋₆alkyl or C₁₋₆alkyloxy; furanyl; furanyl substituted with 1 or 2 substituents selected from C₁₋₆alkyl or hydroxyC₁₋₆alkyl; thienyl; thienyl substituted with 1 or 2 substituents selected from halo or C₁₋₆alkyl; oxazolyl; oxazolyl substituted with 1 or 2 C₁₋₆alkyl substituents; thiazolyl; thiazolyl substituted with 1 or 2 C₁₋₆alkyl substituents; pyridinyl or pyridinyl substituted with 1 or 2 C₁₋₆alkyl substituents;

R¹² is C₁₋₆alkyl or C₁₋₆alkyl substituted with hydroxy, carboxyl or C₁₋₆alkyloxycarbonyl;

Ar¹ is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halo, C₁₋₄alkyl, haloC₁₋₄alkyl, cyano, aminocarbonyl, C₁₋₄alkyloxy and ~~or~~ haloC₁₋₄alkyloxy;

Ar² is naphthalenyl; phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from the group consisting of hydroxy, halo, cyano, nitro, amino, mono- or di(C₁₋₄alkyl)amino, C₁₋₄alkyl, haloC₁₋₄alkyl, C₁₋₄alkyloxy, haloC₁₋₄alkyloxy, carboxyl, C₁₋₄alkyloxycarbonyl, aminocarbonyl and mono- and ~~or~~ di(C₁₋₄alkyl)aminocarbonyl;

Ar³ is phenyl or phenyl substituted with 1, 2 or 3 substituents selected from the group consisting of halo, hydroxy, amino, nitro, aminocarbonyl, C₁₋₆alkyl, haloC₁₋₆alkyl and ~~or~~ C₁₋₆alkyloxy;

Het¹ is a monocyclic heterocycle selected from pyrrolyl, pyrazolyl, imidazolyl, furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyrazinyl and pyridazinyl; or a bicyclic heterocycle selected from the group consisting of quinolyl, quinoxalyl, indolyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, benzofuranyl and benzothienyl; each monocyclic and

bicyclic heterocycle may optionally be substituted on a carbon atom by 1 or 2 substituents selected from the group consisting of halo, C₁₋₄alkyl or mono-, di- ~~and~~ ~~or~~ tri(halo)methyl; and

Het² is a heterocycle selected from the group consisting of 1,4-dihydro-5-oxo-tetrazol-1-yl, imidazo[1,2-a]pyridinyl, oxazolyl ~~and~~ ~~or~~ imidazolyl; each of said heterocycles may be substituted with 1 or where possible 2 substituents selected from the group consisting of C₁₋₄alkyl and Ar³.

2. (Currently Amended) A pharmaceutical composition according to claim 1 wherein, ~~characterized in that~~

L is hydrogen; C₁₋₆alkyl; C₁₋₆alkyl substituted with hydroxy; C₃₋₆alkenyl; Ar³; Ar³C₁₋₆alkyl; di(Ar³)C₁₋₆alkyl; Ar³C₃₋₆alkenyl; di(Ar³)C₁₋₆alkenyl; or a radical of formula (a-1), (a-2), (a-4) or (a-5) wherein :

R⁷ is Ar³; Ar³C₁₋₆alkyl; di(Ar³)C₁₋₆alkyl; C₁₋₆alkyl; C₃₋₇cycloalkyl; C₃₋₇cycloalkyl substituted with Ar³; oxazolyl; oxazolyl substituted with halo or C₁₋₆alkyl; thiazolyl; thiazolyl substituted with halo or C₁₋₆alkyl; imidazolyl; imidazolyl substituted with Ar³, C₁₋₆alkyl, Ar³C₁₋₆alkyl or halo; pyrrolidinyl or furanyl;

Ar³ is is phenyl or phenyl substituted with 1, 2 or 3 substituents selected from halo, hydroxy, amino, aminocarbonyl, C₁₋₆alkyl, haloC₁₋₆alkyl or C₁₋₆alkyloxy;

Het¹ is a monocyclic heterocycle selected from the group consisting of pyrrolyl, pyrazolyl, imidazolyl, furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyrazinyl and pyridazinyl; or a bicyclic heterocycle selected from the group consisting of quinolinyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, benzofuranyl and benzothienyl; each monocyclic and bicyclic heterocycle may optionally be substituted on a carbon atom by 1 or 2 substituents selected from the group consisting of halo, C₁₋₄alkyl or mono-, di- ~~and~~ ~~or~~ tri(halo)methyl.

3. (Currently Amended) A pharmaceutical composition according to claim 1 wherein, ~~any one of claims 1 to 2, characterized in that~~ R¹ is Ar¹methyl and attached to the 2-position or R¹ is Ar¹ and attached to the 3-position.
4. (Currently Amended) A pharmaceutical composition according to claim 1 wherein,

~~any one of claims 1 to 3, characterized in that the R²-X-C(=Q)- moiety is 3,5-di-(trifluoromethyl) phenylcarbonyl.~~

5. (Currently Amended) A pharmaceutical composition according to claim 1 wherein, any one of claims 1 to 4, characterized in that R¹ is Ar¹C₁₋₆alkyl, R² is phenyl substituted with 2 substituents selected from the group consisting of methyl and trifluoromethyl, X is a covalent bond and =Q is =O.
6. (Currently Amended) A pharmaceutical composition according to claim 1 wherein, any one of claims 1 to 5, characterized in that n and m are 1 and p is 1 or 2.
7. (Currently Amended) A pharmaceutical composition according to claim 1 wherein, any one of claims 1 to 6, characterized in that R¹ is phenylmethyl; R² is phenyl substituted with 2 substituents selected from the group consisting of methyl and ~~or~~ trifluoromethyl; n, m and p are 1; X is a covalent bond; and =Q is =O.
8. (Currently Amended) A pharmaceutical composition according to claim 1 wherein, any one of claims 1 to 7, characterized in that L is a radical of formula (a-2) wherein R⁴ is hydrogen or phenyl; r is 0 or 1; Y¹ is a covalent bond, -O- or -NH-; R⁷ is pyrrolidinyl; furanyl; 1-phenylcyclohexanyl; diphenylmethyl; or phenyl substituted with 1, 2 or 3 substituents each independently selected from the group consisting of methyl, methoxy and ~~or~~ chloro
9. (Currently Amended) A pharmaceutical composition according to claim 1 wherein, any one of claims 1 to 8, characterized in that the pharmaceutical composition comprises a compound selected from the group consisting of :
 - ~~⊖~~ 4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-N-(2,6-dimethylphenyl)-1-piperazine acetamide;
 - ~~⊖~~ 4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-N-(1-phenylcyclohexyl)-1-piperazine acetamide;
 - ~~⊖~~ 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-[4-[□-(1-pyrrolidinylcarbonyl)benzyl]-1-piperazinyl]piperidine;
 - ~~⊖~~ 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-[(2-methyl-5-oxazolyl)methyl]-1H-benzimidazol-2-yl]-1-piperazinyl]-2-(phenylmethyl)piperidine;

- ⊖ 4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(4-trifluoromethylphenyl)methyl]-4-piperidinyl]-*N*-(2,6-dimethylphenyl)-1-piperazine acetamide; and
 - ⊖ 4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(3,4-dichlorophenyl)methyl]-4-piperidinyl]-*N*-(2,6-dimethylphenyl)-1-piperazine acetamide.

- 10. (Currently Amended) A pharmaceutical composition according to claim 1 wherein, ~~any one of claims 1 to 8, characterized in that~~ the pharmaceutical composition comprises a compound selected from the group consisting of :
 - ⊖ (+)-(B)-*trans*-4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-*N*-(2,6-dimethylphenyl)-1-piperazine acetamide;
 - ⊖ (-)-(B)-*cis*-4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-*N*-(2,6-dimethylphenyl)-1-piperazine acetamide; and
 - ⊖ (+)-(B)-*trans*-4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-*N*-(2,6-dimethylphenyl)-1-piperazine acetamide (L)-malic acid (1:1).

- 11. (Currently Amended) A pharmaceutical composition according to claim 1 wherein, ~~any one of claims 1 to 6, characterized in that it~~ the pharmaceutical composition is formulated for simultaneous, separate or sequential use.

- 12. (Currently Amended) A pharmaceutical composition according to claim 1 wherein, ~~any of claims 1 to 11, characterized in that~~ the opioid analgesic is one or more compounds selected from the group consisting of alfentanil, buprenorphine, butorphanol, carfentanyl, codeine, diacetylmorphine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanol, lofentanyl, meperidine, methadone, morphine, nalbuphine, oxycodone, oxymorphone, pentazocine, propoxyphene, remifentanyl and sufentanyl; and derivatives and pharmaceutical acceptable salts thereof.

- 13. (Currently Amended) A pharmaceutical composition according to claim 12 wherein ~~characterized in that~~ the opioid analgesic is one or more compounds selected from the group consisting of oxycodone, codeine, morphine, fentanyl, buprenorphine, hydrocodone, hydromorphone and pharmaceutical acceptable salts and derivatives thereof.

14. (Currently Amended) A pharmaceutical composition according to claim 1 ~~where, any one of claims 1 to 13, characterized in that it~~ the pharmaceutical composition is in a form suitable to be orally administered.
15. (Currently Amended) The use of a pharmaceutical composition according to claim 1, ~~any one of claims 1 to 13 for the manufacture of a medicament~~ for the prevention and/or treatment of pain and/or nociception.
16. (Currently Amended) The use of a pharmaceutical composition according to claim 1, ~~any one of claims 1 to 13 for the manufacture of a medicament~~ for the prevention and/or treatment of acute and chronic pain, more in particular in inflammatory, post-operative, emergency room (ER), breakthrough, neuropathic and cancer pain treatments.
17. (Currently Amended) The use of a pharmaceutical composition according to claim 1, ~~any one of claims 1 to 13 for the manufacture of a medicament~~ for the prevention and/or treatment of emesis in opioid-based treatments of pain.
18. (Currently Amended) The use of a pharmaceutical composition according to claim 17 ~~for the manufacture of a medicament~~ for the prevention and/or treatment of nausea and vomiting in opioid-based treatments of pain.
19. (Currently Amended) The use of an NK₁-receptor antagonist, in particular an NK₁-receptor antagonist according to Formula (I), the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the *N*-oxide form thereof and prodrugs thereof, ~~for the manufacture of a medicament~~ for the prevention and/or treatment of respiratory depression in opioid-based treatments of pain.
20. (Currently Amendment) The use of an NK₁-receptor antagonist, in particular an NK₁-receptor antagonist according to Formula (I), the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the *N*-oxide form thereof and prodrugs thereof, ~~for the manufacture of a medicament~~ for reducing and/or overcoming the tolerance observed with opioids in opioid-based treatments of pain.